REMARKS

Claims 1-11 are pending. Claims 1-6 and 10-11 have been withdrawn pursuant to a previous Restriction Requirement. Claims 7-9 are objected and rejected. Applicants respectfully request reconsideration of claims 7-9 in view of the claim amendments and the following remarks.

The amended paragraph [0035] of the published specification corrects a typographical error and does not introduce any new matter.

Paragraphs [0081], [0084]-[0085], [0089], [0092]-[0093], [0095]-[0096], [0098] and [0101] of the published specification have been amended because the submitted drawings are black-and-white, thus the descriptions referring to color have been deleted. No new matter is introduced with these amendments.

Response to Drawing Objection

The drawings have been objected to on the basis that they might have been submitted as color drawings. Applicants respectfully note that the drawings were submitted as black-and-white drawings in the original application, thus rendering the Examiner's objection moot.

Response to Claim Objections

Claims 7-9 have been objected to because of informalities. Claims 7-9 have been amended to correct these informalities thus the Examiner's objections are now rendered moot.

Response to 35 U.S.C. §112, First Paragraph Rejection

Claims 7-9 have been rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement. The Examiner argues that the specification does not provide sufficient description for a genus of genes possessing the biological characteristics of an AMPA-type glutamate receptor subunit GluR2. The Examiner contends that the applicants were not in possession of the claimed invention at the time of filing this application. Applicants respectfully disagree with the rejection.

AMPA-type glutamate receptors are described in paragraphs 5-9 of the published specification. Prior to submission of this application it was determined that glutamate receptors, including AMPA-type glutamate receptors, are present in glial cells (see paragraph 11 of the published specification). The information provided by applicants in the instant publication provide support for the invention disclosed in claims 7-9 which provide a method of inhibiting proliferation and invasion of brain tumor cells by regulating the Ca^{2+} permeability by AMPA-type glutamate receptor subunits (see paragraphs 15, 38-39, 43-45, 47-51, 55, and 58-59, Table 1, and Figure 3 of the published specification).

Furthermore, as stated in the instant specification, the gene of the AMPA-type glutamate receptor subunit GluR2 was deposited in GenBank under Accession No. M38061. Therefore, one of ordinary skill in the art would be able to ascertain the gene that is disclosed in claims 7-9 to use for the treatment of brain tumors from reading the instant specification and from what was commonly known in the art. Although applicants assert that the instant specification has sufficient written description, claim 7 has been amended solely to further prosecution of the present application. Support for

the GenBank Accession number may be found at paragraph 26 of the published specification.

Reconsideration and withdrawal of the rejections under 35 U.S.C. §112, first paragraph, of the presently amended independent claim 7 and presently amended dependent claims 8 and 9 are respectfully requested.

Response to 35 U.S.C. §102(b) Rejections

Claims 7-9 have been rejected under 35 U.S.C. §102(b) as being anticipated by Ishiuchi et al. (*NeuroReport* 12:745-748). The Examiner contends that Ishiuchi et al. describes recombinant adenoviruses containing the GluR2 coding sequence; however, the use of gene expression vectors for treating brain tumors was not anticipated.

Applicants respectfully traverse the Examiner's contention that Ishiuchi et al. describes the basic effect that GluR2 has on glial cells. Ishiuchi does not describe using GluR2 expression vectors to treat brain tumors.

As the Examiner is well aware, for a reference to anticipate a claim it must teach every element of the claim (*See* MPEP §2131). An essential feature of claim 7 is that GluR2 is introduced into tumor cells to destroy brain tumors by inhibiting cellular migration and promoting cellular apoptosis. Claims 8 and 9 are dependent on claim 7.

Ishiuchi et al. merely discloses the change in cellular morphology that occurs to **normal** glial cells when adenoviruses containing the GluR2 gene are introduced. In the specification, applicants provide a description of the inhibitory effects on cell migration and onset of cellular apoptosis when GluR2(R) genes are introduced into **tumor** cells (see paragraph 15). Ishiuchi et al. evaluated the morphological changes in normal glial

cells in order to study the role of glutamate in neuronal-glial interactions. (*NeuroReport*, p. 748). One of ordinary skill in the art would not anticipate the inhibition of cellular migration or the onset of apoptosis of **tumor** cells by the introduction of GluR2 genes based on the Ishiuchi et al. publication.

Furthermore, Ishiuchi et al. discloses *in vitro* experimentation of GluR2 delivery to cells by adenoviruses. Applicants herein provide a specification that discloses the results and conclusions of *in vivo* experiments using a nude mouse model of human glioblastoma (see paragraphs 57-60 of the published specification). *In vitro* experimentation can only provide the basic information about biological process, but must be followed by *in vitro* experimentation for further clarification and confirmation. Based on the Ishiuchi et al. publication one of ordinary skill in the art would have to partake in undue experimentation to confirm that the introduction of GluR2 to cells has the same effect *in vivo*. Applicants took this basic information provided by the Ishiuchi et al. publication and applied it to an *in vitro* model to confirm this effect. Furthermore, they applied this information to tumor cells. Applicants describe the inhibitory effect on cellular migration as well as the apoptotic effect that GluR2 gene has when introduced to tumor cells. This further experimentation was needed to confirm the effects that GluR2 gene introduction has on cellular processes and also provides information about the effects of GluR2 on tumor cells. None of this information is provided by the Ishiuchi et al. publication.

Applicants provide further insight into the role of GluR2 in cellular interactions *in vivo*. One of ordinary skill in the art would not anticipate that an increase in GluR2 genes within a tumor cell would increase the onset of cellular apoptosis based on the

information provided in Ishiuchi et al. It is general knowledge that cellular apoptosis is defective in most cancer cells (*See* Molecular Biology of the Cell, 4th Ed., Alberts et al., p. 1322 (2002)). While one of ordinary skill in the art may anticipate that an alteration of the Ca^{2+} permeability by an increase in GluR2 may induce apoptosis in a normal cell, it is unexpected to find that the increase in GluR2 can induce apoptosis in tumor cells. Applicants disclose this effect of GluR2 in the specification making claims 7-9 novel.

Applicants respectfully request reconsideration and withdrawal of the §102(b) rejections for the above reasons.

Response to 35 U.S.C. §103(a) Rejections

Claims 7-9 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Heinemann et al. (U.S. 5,202,257) taken with Shine et al. (WO 97/17090). Applicants respectfully traverse this rejection.

Neither Heinemann nor Shine, alone or in combination teach an essential feature of claims 7-9, i.e. the application of the GluR2 gene to destroy tumor cells for the treatment of brain tumors. Heinemann describes cDNA encoding the GluR2 gene and its use as probes for genetic screening. The Examiner admits that Heinemann does not teach an adenoviral vector comprising the GluR2 cDNA. Shine describes the use of adenoviral vectors to produce bioactive compounds for therapeutic purposes. The Examiner contends that it "would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Heinemann with Shine, namely to produce an adenoviral vector comprising cDNA encoding GluR2" (see Office Action dated July 27, 2006 – page 7). However, applicants assert that the

Examiner has used hindsight in combining Heinemann and Shine. Specifically, the Examiner contends that the skilled artisan would be motivated to use adenoviral vectors to produce proteins. However, there are a multitude of ways to produce proteins including other gene expression vectors such as the use of retrovirals (i.e. MMLV, Lentiviral, etc.). There is no teaching in Heinemann to direct or provide guidance to one skilled in the art to select the use of adenoviral vectors as described in Shine over any of the other means to produce proteins. Therefore, applicants respectfully assert that there is no motivation to combine Heinemann and Shine and the combination of these two references would not teach one of ordinary skill in the art to use an adenoviral vector to introduce GluR2 genes into tumor cells for the treatment of brain tumors.

Applicants respectfully request reconsideration and withdrawal of the §103(a) rejections to claims 7-9 for the above reasons.

CONCLUSION

Applicants respectfully request reconsideration of the amended claims and urge that the present claims are in condition for allowance. Early and favorable action is earnestly solicited.

AUTHORIZATION

The Commissioner is hereby authorized to charge any additional fees which may be required for this response, or credit any overpayment to Deposit Account No. 13-4500, Order No. 4439-4030.

In the event that an extension of time is required, or which may be required in addition to that requested in a petition and for an extension of time, the Commissioner is requested to grant a petition for that extension of time which is required to make this response timely and is hereby authorized to charge any fee for such an extension of time or credit any overpayment for an extension of time to Deposit Account No. 13-4500, Order No. 4439-4030.

Respectfully submitted,

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Dated: October 24, 2006

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